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Committee for Medicinal Products for Human use (CHMP)

Concept paper on the need for revision of the guideline on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis

Agreed by Rheumatology/Immunology Working Party	August 2012
Adopted by CHMP for release for consultation	06 September 2012
Start of public consultation	01 October 2012
End of consultation (deadline for comments)	15 December 2012

The proposed guideline will replace the guideline on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis (CPMP/EWP/422/04)

Comments should be provided using this template. The completed comments form should be sent to RIWPsecretariat@ema.europa.eu

Keywords	Juvenile idiopathic arthritis, Systemic JIA, Oligoarthritis, Polyarthritis, Enthesitis related arthritis, Extrapolation

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1. Introduction

The current CHMP Guideline on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis (JIA) was adopted by CHMP in 2006. Since then there have been major advances in the understanding of the pathophysiology of JIA subtypes, along with the introduction of new treatments including biological therapies. The Paediatric committee (PDCO) at the EMA have reviewed multiple paediatric investigation plans (PIPs) for JIA as a result of the Paediatric Regulation. Accumulated experience has highlighted the need for a revision of the requirements for demonstration of efficacy in JIA. Some extrapolation from efficacy results in adults to certain subtypes of JIA is possible.

In addition new validated methods for assessment of disease activity and joint damage have been developed. As a result of the advances in therapeutics, the treatment paradigm for JIA has changed such that rapid treatment initiation following early diagnosis is practiced in order to minimise joint damage.

Therefore, updating the current JIA guidelines is required to reflect these recent advances.

2. Problem statement

As a result of recent advances in classification, diagnosis and treatment the JIA guidelines needs to be updated with particular emphasis on the following:

- Paediatric investigation plans
- Included populations
- Age range in different subtypes
- Feasibility issues affecting paediatric development
- Extrapolation from adults
- Study design, primary endpoints
- Active comparator
- Assessment of structural damage
- Treatment discontinuation, safety and efficacy of re-treatment
- Definition of flare and remission
- Paediatric-specific complications of JIA and treatments
- Inclusion of JIA uveitis in JIA studies
- Long-term follow-up and registries

3. Discussion (on the problem statement)

A consistent approach to PIP development is required that will serve as the basis for marketing authorisation applications.

The currently used ILAR (International League Against Rheumatism) classification distinguishes JIA subtypes which are mutually exclusive and patients should be classified using the ILAR criteria[1].

Juvenile idiopathic arthritis consists of subtypes the majority of which have counterparts in the more frequent adult diseases of rheumatoid arthritis, spondyloarthritis and psoriatic arthritis.

Chronic idiopathic arthritis should be used as the name of the condition for PIPs for medicines for juvenile idiopathic arthritis (JIA). This condition would include rheumatoid arthritis, psoriatic arthritis, and spondyloarthritis in adults and juvenile idiopathic arthritis (JIA) in children. Whenever development is considered in any of the three adult diseases, in principle a PIP is required for JIA[2].

The efficacy of the agents should be evaluated by subtype to reflect the potential differences in response among the categories distinguished by the ILAR criteria.

In order to facilitate translation of clinical trial results into routine clinical care four target JIA patient populations have been identified with distinctive clinical courses and therapeutic approaches (Beukelman et al)[3].

- Systemic onset JIA (with or without current systemic features)
- Polyarticular course JIA (4 or more joints involved in the course of the disease, all ILAR groups except systemic JIA and enthesitis related arthritis
- Oligoarticular course JIA (maximum 3 joints involved in the course of the disease, no sJIA and no ERA)
- Enthesitis related arthritis (ERA, as per ILAR classification)

When conducting trials in JIA this clinical grouping where possible is advised in order to enable simpler and smaller subsets that are more clinically homogenous and reflective of current practice[1].

Treatment of JIA uveitis has not been addressed sufficiently in development of medicines for JIA. This unmet medical need needs to be addressed in PIPs for JIA.

The revision to the JIA guidelines will focus on updating the points listed under the problem statement.

4. Recommendation

It is proposed to update the CHMP Guideline addressing the clinical investigation of medicinal products for the treatment of JIA in order to achieve a European common position on the above-mentioned issues.

5. Proposed timetable

It is anticipated that a new draft CHMP Guideline will be available within 6 months after adoption of the concept paper. The draft CHMP guideline will then be released for 6 months for external consultation and following receipt of comments it will be finalised in approximately 3 months.

6. Resource requirements for preparation

The preparation of this Guideline will involve the Rheumatology/Immunology Working Party, including one Rapporteur and one Co-Rapporteur. Close cooperation with PDCO is envisioned. It is anticipated that at least three plenary session discussions at the RIWP will be needed.

7. Impact assessment (anticipated)

The elaboration of the Guideline on clinical investigation of medicinal products for the treatment of JIA will be helpful to achieve consensus in the evaluation of such products by regulatory authorities while accommodating advances in clinical practice. Furthermore, it is expected that such guidance document would improve quality and comparability of submitted studies by pharmaceutical industries.

8. Interested parties

European League Against Rheumatism (EULAR)

Paediatric Rheumatology International Trials Organisation (PRINTO)

Paediatric Rheumatology European Society (PRES)

9. References to literature, guidelines, etc.

1. Petty RE et al.: International League of associations for rheumatology Classification of Juvenile Idiopathic Arthritis: Second Revision, Edmonton, 2001; J Rheumatol (2004) 31:2, 390-392

2. Paediatric Rheumatology Expert Group Meeting at EMA (EMA/836276/2010) http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/03/WC500103514.pdf

3. Beukelman T et al. 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Initiation and Safety Monitoring of Therapeutic Agents for the Treatment of Arthritis and Systemic Features. Arthritis Care & Research Vol. 63, No. 4, April 2011, pp 465–482